

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 November 2002 (21.11.2002)

PCT

(10) International Publication Number
WO 02/092588 A3

(51) International Patent Classification: C07D 309/08,
405/12, 401/12, 211/66, 407/12, 417/12, 409/12, 413/12,
A61K 31/351, A61P 35/00

(21) International Application Number: PCT/US02/15257

(22) International Filing Date: 10 May 2002 (10.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/290,375 11 May 2001 (11.05.2001) US

(71) Applicant (for all designated States except US): PHAR-
MACIA CORPORATION [US/US]; Corporate Patent
Department, 800 North Lindbergh Blvd., Mail Zone 04E,
St. Louis, MO 63167 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BARTA, Thomas,
E. [US/US]; Apt. 3-W, 1133 Maple Avenue, Evanston,
IL 60202 (US). BECKER, Daniel, P. [US/US]; 1800
Maplewood Lane, Glenview, IL 60025 (US). BEDELL,
Louis, J. [US/US]; 208 E. Marion Avenue, Mt. Prospect,
IL 60070 (US). BOEHM, Terri, L. [US/US]; 928 Cleta
Drive, Ballwin, MO 63021 (US). FOBIA, Yvette, M.
[US/US]; 580 Eagles Nest Ct., Wildwood, MO 63011
(US). FRESKOS, John, N. [US/US]; 7572 York, Clayton,
MO 63105 (US). HOCKERMAN, Susan L. [US/US];
5319 W. Hutchinson, Chicago, IL 60641 (US). KASSAB,
Darren, J. [US/US]; 16346 Centerfield Court, Apt. E,
Wildwood, MO 63040 (US). KOLODZIEJ, Steve, A.
[US/US]; 2448 Clarjon Drive, Ballwin, MO 63021 (US).
MCDONALD, Joseph, J. [US/US]; 1716 Timber Ridge
Estate Dr., Wildwood, MO 63011 (US). NORTON,
Monica, B. [US/US]; 7777 Gissler Avenue, St. Louis, MO

63117 (US). RICO, Joseph, G. [US/US]; 524 Wetherby
Terr. Dr., Ballwin, MO 63021 (US). TALLEY, John, J.
[US/US]; 5 Marlborough Street #5, Boston, MA 02116
(US). VILLAMIL, Clara, L. [US/US]; 813 Long Road,
Glenview, IL 60025 (US). WANG, Tijuana, Jane [CN/US];
919 Crown Pointe Est. Dr., Wildwood, MO 63021 (US).

(74) Agent: GRYTE, David, M.; 800 N. Lindbergh Blvd., St.
Louis, MO 63167 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
27 February 2003

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

Atty. Docket No. 3589/1/US
Serial No. 10/807,884
Babiak et al.
Reference 32

(54) Title: AROMATIC SULFONE HYDROXAMATES AND THEIR USE AS PROTEASE INHIBITORS

(57) Abstract: This invention is directed to aromatic sulfone hydroxamates (also known as "aromatic sulfone hydroxamic acids") and salts thereof that, *inter alia*, inhibit matrix metalloproteinase (also known as "matrix metalloprotease" or "MMP") activity and/or aggrecanase activity. This invention also is directed to a prevention or treatment method that comprises administering such a compound or salt in an MMP-inhibiting and/or aggrecanase-inhibiting effective amount to an animal, particularly a mammal having (or disposed to having) a pathological condition associated with MMP and/or aggrecanase activity.

WO 02/092588 A3

BEST AVAILABLE COPY

EV 317349941 US

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 02/15257

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D309/08 C07D405/12 C07D401/12 C07D211/66 C07D407/12
 C07D417/12 C07D409/12 C07D413/12 A61K31/351 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 50396 A (SEARLE) 31 August 2000 (2000-08-31) claims; example 398	1-6, 380-405
X	WO 00 69821 A (SEARLE) 23 November 2000 (2000-11-23) claims	1-6, 380-405
X	WO 99 25687 A (SEARLE) 27 May 1999 (1999-05-27) page 521 -page 535; claims 1-15; table 123	1-6, 237, 238, 380-405

☐ Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

11 December 2002

Date of mailing of the international search report

23/12/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentkan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax (+31-70) 340-3016

Authorized officer

Francois, J

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/15257

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 380 to 401 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 8.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ASA/ 210

Continuation of Box I.2

Present claims .1 to 5,122,123,225,226,235,236,250,251,260,261,267,268,296,297,303,304,308,309,322,323,335 to 338,344,345,354,355,359 to 362,368,369,372,373,376,377 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds where A2 and A3 together with the carbon to which they are both attached, form an optionally-substituted piperidino or tetrahydropyrano group.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 02/15257

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0050396	A	31-08-2000	US 2001039287 A1	08-11-2001
			AU 3478500 A	14-09-2000
			BR 0008491 A	17-09-2002
			CN 1370144 T	18-09-2002
			CZ 20013038 A3	17-07-2002
			EP 1230219 A1	14-08-2002
			HU 0200239 A2	29-06-2002
			JP 2002537378 A	05-11-2002
			NO 20013963 A	23-10-2001
			NZ 513648 A	28-09-2001
			WO 0050396 A1	31-08-2000
WO 0069821	A	23-11-2000	AU 4797000 A	05-12-2000
			EP 1183239 A1	06-03-2002
			HU 0201680 A2	28-09-2002
			NO 20015543 A	10-01-2002
			WO 0069821 A1	23-11-2000
WO 9925687	A	27-05-1999	AU 1373299 A	07-06-1999
			BR 9814643 A	03-10-2000
			CA 2306460 A1	27-05-1999
			CN 1279669 T	10-01-2001
			EP 1042290 A1	11-10-2000
			JP 2001523662 T	27-11-2001
			NO 20002469 A	12-07-2000
			NZ 503485 A	25-10-2002
			PL 341379 A1	09-04-2001
			WO 9925687 A1	27-05-1999
			US 2001014688 A1	16-08-2001
			US 2001039287 A1	08-11-2001
			ZA 9810412 A	09-12-1999